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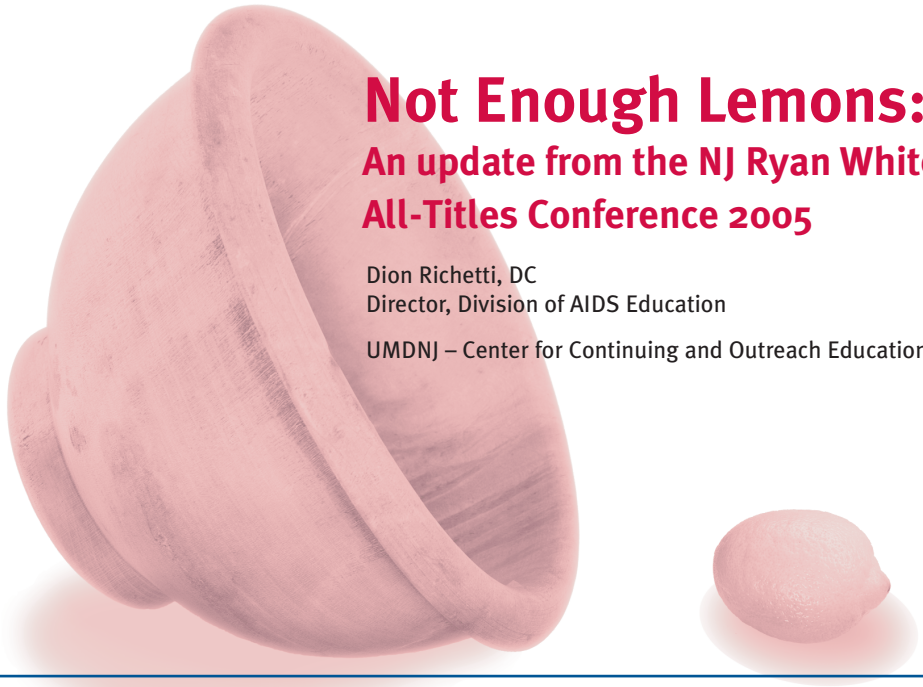
Director's Message



Not Enough Lemons:

An update from the NJ Ryan White All-Titles Conference 2005

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UMDNJ – Center for Continuing and Outreach Education

On November 15th, 2005, 170 people came together at Rutgers University's Busch Campus Center to learn more about and discuss the current state of the Ryan White CARE Act in New Jersey. The forum for this activity was the New Jersey Ryan White All-Titles Conference (the fourth of a series of biannual events sponsored by the NJ Department of Health and Senior Services, Division of HIV/AIDS Services and the Division of AIDS Education at UMDNJ). This diverse group included persons people living with HIV, nurses, physicians, case managers, healthcare administrators, state health officials and others. Eighty-six of them completed an evaluation form that almost unanimously said one thing: we need more information on what other resources there are for people living with HIV in our state!

This conference, which I wrote about in this space in the Spring 2005 issue *(NJ AIDSLine, Volume 1, Number 4: Making Lemonade: The 2005 NJ Ryan White All-Titles Conference)*, was planned by the New Jersey Statewide Coordinated Statement of Need Planning Task Force (SCSN PTF). In developing the conference, the Task Force realized that whether or not the CARE Act is reauthorized, there are more people living with HIV in our state than there are adequate resources to support them. The SCSN PTF developed an ambitious agenda that included among its objectives: "to address the availability of non-Ryan White-funded resources in New Jersey." Participants signed up for the conference hoping to find new ways to help their clients access services. The program included a series of concurrent workshops that were designed in part to accomplish this objective.

What many of us heard was that in some ways, the person living with HIV has more available to them than people in similar socioeconomic conditions, simply because they are HIV-positive. We hoped to hear some "trade secrets" from individuals identified as experts with many years of experience in their respective fields. By the end of the day, many of us did learn some new tricks and some very specific ideas as to how to develop housing opportunities for clients.

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CME

Update on HIV and Hepatitis C Virus Co-Infection: CME Credit Information

Target Audience

This activity is designed for physicians and nurses, and for other health care professionals who are involved in the care of individuals with HIV infection.

Statement of Need

Hepatitis C (HCV) is a common and serious co-infection found in HIV-infected patients, with estimates ranging from 25% in national studies to between 50% and 90% among people with a history of intravenous drug use, the most common HIV transmission mode in New Jersey.

People who are co-infected with HIV and HCV have an accelerated course of HCV infection and liver disease, with 15-25% progressing to cirrhosis compared to 3-6% of HCV mono-infected patients.

HCV treatment is challenging for both clinicians and patients, as there are limited treatment options, and many patients experience serious side effects making treatment contraindicated or intolerable. Among patients who complete a 48-week course of treatment with the recommended regimen of pegylated interferon and ribavirin, estimates of treatment success, measured by sustained viral response (SVR), or success in clearing HCV, range from 27% to 44%.

Clinicians need to make complex assessments of patients' readiness and appropriateness for HCV treatment based on their liver functions and symptoms, stability of HIV disease management, HIV treatment adherence, and pre-existing mental health conditions. Assessment of patients with HCV includes clinical examination, antibody testing, qualitative and quantitative RNA assays, HCV genotyping, liver biopsy, and additional evaluation of liver enzymes and blood counts.

Although all patients with HIV and chronic HCV infection should be considered for HCV antiviral therapy, many will not be good candidates at the time of assessment.

Treatment for HIV and HCV must be carefully coordinated or co-managed to reduce interactions and toxicities, and assure effectiveness of treatment for both diseases.

Learning Objectives

Upon the completion of this activity, participants should be able:

- To describe the epidemiology and natural history of HIV/HCV co-infection.
- To recognize the role of laboratory testing for the diagnosis and ongoing monitoring of HCV in HIV-infected patients.
- To identify HCV treatment candidates and implement evidence-based treatment regimens for the management of HCV in HIV co-infected patients.

Method of Instruction

Participants should read the learning objectives and review the activity in its entirety. After reviewing the material, complete the self-assessment test consisting of a series of multiple-choice and True/False questions.

Upon completing this activity as designed and achieving a passing score of 70% or more on the self-assessment test, participants will receive a CME credit letter awarding AMA/PRA category 1 credit and the test answer key four (4) weeks after receipt of the self-assessment test, registration, and evaluation materials.

Estimated time to complete this activity as designed is 1 hour.

UMDNJ–Center for Continuing and Outreach Education is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UMDNJ–Center for Continuing and Outreach Education designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

The activity was prepared in accordance with the ACCME Essentials.

This activity was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Dion Richetti, DC and Patricia Kloser, MD, MPH

Faculty

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Disclosure

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, all program faculty are required to disclose to the activity participants: 1) the existence of any financial interest or other relationships with the manufacturers of any commercial products/devices, or providers of commercial services, that relate to the content of their presentation/material, or the commercial contributors of this activity, that could be perceived as a real or apparent conflict of interest; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/ device not yet approved.

Faculty Disclosure Declarations

Patricia Kloser, MD, MPH (Field Tester and Activity Director) has the following financial relationships to disclose: Speaker's Bureau: GlaxoSmithKline, Roche, Glaxo; Consultant: Gilead, Boehringer Ingleheim.

The faculty listed below declare that they have no financial relationships with any corporate organization whose product(s) will be discussed in this presentation:

Mona Bhatt Shah, MD, MPH, Sindy M. Paul, MD, MPH, Eliahu Bishburg, MD, Eugene G. Martin, PhD, and Shobha Swaminathan, MD

Off-Label Usage Disclosure

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Disclaimer:

The views expressed in this activity are those of the faculty. It should not be inferred or assumed that they are expressing the views of NJDHSS-Division of HIV/AIDS Services, UMDNJ, or any manufacturer of pharmaceuticals.

The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult the full prescribing information on any agent(s) presented in this activity for recommended dosage, indications, contraindications, warnings, precautions, and adverse effects before prescribing any medication. This is particularly important when a drug is new or infrequently prescribed.

Grantor Acknowledgement

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University of Medicine and Dentistry of New Jersey

Center for Continuing & Outreach Education
Division of AIDS Education

A Local Performance Site of the NY/NJ AETC

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Update on HIV and Hepatitis C Virus Co-Infection

Mona Bhatt Shah, M.D., M.P.H.; Sindy M. Paul, M.D., M.P.H.; Eliahu Bishburg, M.D.; and Eugene G. Martin, Ph.D.

CME

Learning Objectives:

- To describe the epidemiology and natural history of HIV/HCV co-infection.
- To recognize the role of laboratory testing for the diagnosis and ongoing monitoring of HCV in HIV-infected patients.
- To identify HCV treatment candidates and implement evidence-based treatment regimens for the management of HCV in HIV co-infected patients.

Introduction

Since the 1996 introduction of highly active antiretroviral therapy (HAART) and its contribution to longer life expectancies in patients with HIV disease, the hepatitis C virus (HCV) has become an increasingly important cause of morbidity and mortality in HIV-infected individuals.[1] Chronic liver disease is now the leading non-AIDS cause of death in co-infected individuals with HIV.[2]

With an estimated prevalence of 1.8% of the population, HCV is the most common, chronic blood-borne infection in the U.S.[3] According to the Centers for Disease Control and Prevention (CDC), there are an estimated 2.7 million people living with chronic hepatitis C infection.[4]

There are approximately 1.0-1.2 million people living with HIV/AIDS in the U.S.[5] In one study, the prevalence of HCV/HIV co-infection was found to be 16.1%, but the CDC estimated the actual prevalence of HCV infection at 25% of HIV-positive people in the U.S.[2, 6-7] The HCV co-infection prevalence among HIV-positive people may be as high as 50% to 90% in populations such as injection drug users and hemophiliacs in the U.S.[7-8]

Although the increasing clinical importance of co-infection has become clearer in the past several years, treatment options remained limited. Until recently, interferon-alfa combined with ribavirin was the sole treatment option available for chronic hepatitis C in patients co-infected with HIV. This treatment had a very low rate of effectiveness, and was associated with extensive side effects . Over the past year, four large clinical trials evaluating the combination of pegylated interferon and ribavirin have had promising results in treating HIV/HCV co-infected patients. Rates of treatment success, measured by sustained virologic response (SVR) of undetectable HCV-RNA following treatment, were reported at 27-44% , with additional patients showing slowed progression of liver disease. As a result, in February 2005, the FDA approved pegylated interferon-a-2a (Pegasys®) and ribavirin (Copegasus®), both marketed by Roche, for treatment of chronic hepatitis C in HIV/HCV co-infected patients.[9]

HCV/HIV Co-Infection

Hepatitis C Disease

Hepatitis C is caused by the hepatitis C virus, which is a single-stranded RNA virus of the Flaviviridae family. Six unique HCV genotypes with 50 subtypes have been identified to date. Infection with HCV genotype 1 accounts for an estimated 75% of HCV-infected individuals in the U.S., and of all the genotypes, genotype 1 has the poorest treatment response.[8]

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Transmission

HCV transmission occurs mainly through infected blood or blood products. Currently, the primary route of acquisition in the U.S. is through injection drug use. Prior to 1992, the predominant mode of transmission was transfusion-related. Other transmission routes include vertical, sexual, and needle stick injuries. HCV transmission from mother to child accounts for an estimated 5% of HCV spread, but this estimate increases to 17% if the mother is infected with HIV.[8] Sexual transmission rates in monogamous couples are low (‹1%); however, these rates are thought to be higher (5%-10%) in men who have sex with men.[10-11]

Pathogenesis and Natural History

HIV appears to hasten the natural history of HCV infection. Patients with HIV/HCV co-infection have higher blood levels of HCV RNA, an accelerated progression of liver disease, and a greater rate of hepatitis-related deaths than patients who have HCV infection alone.[12-13] The pathogenesis of accelerated progression is poorly understood. HIV may have a direct cytopathic effect on liver cells and may also aid in infecting extrahepatic cells.[12] The increased HCV viremia is attributed to the loss of CD4+ T lymphocytes in HIV-infected patients.[12] Spontaneous clearance of HCV occurs in 15%-30% of cases in mono-infected patients vs. 5%-10% for co-infected patients.[7,14]

The risk for progressive liver disease is estimated to be 2.9 times higher among HIV/HCV co-infected individuals compared to HCV mono-infected patients.[8] Progression to cirrhosis occurs in 15%-25% of co-infected patients as compared to 3%-6% of HCV mono-infected patients.[14-15] This progression generally takes 20 to 30 years in HCV mono-infected patients and is accelerated to 6 to 10 years in co-infected individuals.[16] Hepatocellular carcinoma (HCC) occurs at a younger age and after a shorter duration of HCV infection, and once cirrhosis is established, the rate of progression to HCC is 1%-4% per year.[14,17] The time from infection to HCC has been demonstrated to occur 10 years earlier in co-infected patients (from 28 to 18 years).[18] Factors such as alcohol use and older age also increase the rate of liver fibrosis progression.[19]

Whether HCV impacts the rate of progression of HIV infection is uncertain. Limited studies have found that HCV may increase morbidity and mortality in HIV infected patients on HAART.[20-21] In the Swiss HIV cohort study, it was shown that the clinical progression to AIDS at 2 years was 6.6% in HIV mono-infected individuals as compared to 9.7% in co-infected patients.[20] A meta-analysis study by Miller and colleagues found that co-infected patients had a diminished rise in the CD4 cell count when they begin HAART as compared to HIV mono-infected patients.[22] However, further follow-up studies of patients on HAART suggest that there may not be a difference in HIV-related mortality between patients co-infected with HCV and patients infected with HIV alone.[12]

Clinical Manifestations

HCV infection is responsible for approximately 15% of acute viral hepatitis, 60-70% of chronic hepatitis, 50% of cirrhosis, end-stage liver disease, and liver cancer, and for 10,000 to 12,000 deaths annually in the U.S.[23] Because its presentation is often asymptomatic or mildly symptomatic, acute hepatitis is often not diagnosed. Symptoms of acute infection include low-grade fever, mild right-upper-quadrant pain, nausea, vomiting, anorexia, dark urine, and jaundice.[8]

Symptoms of chronic hepatitis C range from no symptoms at all to mild, nonspecific symptoms, which include fatigue, mild right-upper-quadrant tenderness, nausea, poor appetite, and muscle and joint pain.[23] As the disease progresses into cirrhosis, patients may present with muscle weakness, weight loss, itching, dark urine, fluid retention, and abdominal swelling.[23] Signs of portal hypertension such as spider angiomata, temporal wasting, splenomegaly, caput medusa, and encephalopathy may also be present.[8] Occasionally, some patients experience cutaneous manifestations such as leukocytoclastic vasculitis and porphyria cutanea tarda.[8]

Physical examination of patients with chronic hepatitis C may reveal mild hepatomegaly. Patients who have cirrhosis may have hepatomegaly, splenomegaly, jaundice, muscle wasting, excoriations, ascites, and ankle edema on examination.[23] Other hepatic manifestations of HCV include fulminant hepatitis and hepatocellular carcinoma

Table 1. Persons for Whom HCV Testing is Recommended

- Persons who have injected illicit drugs in the recent and remote past, including those who injected only once and do not consider themselves to be drug users
- Persons with conditions associated with a high prevalence of HCV infection, including:
  - Persons with HIV infection
  - Persons with hemophilia who received clotting factor concentrates before 1987
  - Persons who were ever on hemodialysis
  - Persons with unexplained abnormal aminotransferase levels
- Prior recipients of transfusions or organ transplants, including:
  - Persons who were notified that they had received blood from a donor who later tested positive for HCV infection
  - Persons who received a transfusion of blood or blood products before July 1992
  - Persons who received an organ transplant before July 1992
- Children born to HCV-infected mothers
- Health care, emergency medical and public safety workers after a needle stick injury or mucosal exposure to HCV-positive blood
- Current sexual partners of HCV-infected persons*

NOTE. Table adapted from Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic diseases. MMWR Recomm Rep. 1998; 47 (RR-19):1-39.

*Although the prevalence of infection is low, a negative test in the partner provides reassurance, making testing of sexual partners of benefit in clinical practice.

(often asymptomatic). Extrahepatic manifestations of HCV occur in 1-2% of patients and commonly include mixed cryoglobulinemia, glomerulonephritis, Sjogren syndrome, and hypothyroidism especially in women.[24]

Diagnostic Testing

Who Should Be Tested?

Current guidelines supported by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) recommend that the detection of HCV infection is best accomplished by screening populations for risk factors and then testing identified, high-risk individuals (see Table 1).[25] Through careful questioning, an HCV risk factor can be found in more than 90% of cases.[25] Because of the high prevalence of HCV in HIV-infected patients, all patients with HIV should be tested for anti-HCV antibody.[3]

Laboratory Evaluation

The 2004 guidelines from the CDC, the NIH, and the HIV Medicine Association/IDSA on the treatment of opportunistic infections among HIV-infected adults and adolescents recommend that HIV patients be tested first for antibody to HCV using the most sensitive enzyme immunoassay (EIA) licensed for the detection of HCV antibody, and if positive confirmed utilizing a qualitative HCV ribonucleic acid (RNA) assay with a lower detection limit of ≤50 IU/mL. Additional, more specific testing for HCV antibody by recombinant immunoblot assay can be used as a subsequent confirmatory method if the HCV RNA is negative and the EIA is positive (See Figure 1).[8] Such findings occur occasionally in patients who have recovered from acute hepatitis C and are no longer viremic and occasionally among patients whose HCV RNA levels transiently decline below the detection level of the assay.

Enzyme Immunoassay

Enzyme immunoassays were originally developed as an alternative to radioisotopes. EIAs achieve their signal through the catalytic reaction of enzymes. There are many innovative formats in use. In the U.S., a third generation EIA is in use but because of sensitivity/specificity issues, a confirmatory test is needed to ensure appropriate specificity of a positive finding.[10] A negative HCV antibody result generally excludes the diagnosis of HCV with the following exceptions: acute HCV infection in the antibody 'window' or immunosuppressed states. In 30%-40% of patients, anti-HCV is not detected until 2 to 8 weeks after the onset of symptoms.[23,25] Patients with acute hepatitis and patients who are co-infected with HIV with suspected liver disease and who test negative for anti-HCV antibody should be re-tested using the HCV RNA assay, primarily because it reduces the window of viral detection.[23,25]

Qualitative and Quantitative Assays for HCV RNA

HCV RNA levels can be detected within 1 to 2 weeks of infection.[25] Both qualitative and quantitative HCV RNA assays can be utilized. Many clinicians prefer a quantitative assay rather than qualitative test, because the test measures the amount of HCV RNA, which is useful for initiating and monitoring treatment. Qualitative assays are designed to be more sensitive than the quantitative assays, so some experts recommend that the qualitative HCV RNA test be used as the initial test or to confirm a positive HCV antibody test when there is a negative quantitative HCV RNA assay.[25]

Qualitative nucleic amplification assays for HCV RNA utilize either a polymerase chain reaction (PCR) or transcription mediated amplification (TMA) technique. The PCR-based tests are able to detect HCV RNA in serum down to a lower limit of 50 IU/ml, and the TMA-based assays are able to identify HCV RNA in serum down to a lower limit of 9.6 IU/mL.[25]

Quantitative assays for HCV RNA utilize either a target amplification technique (PCR, TMA) or a signal amplification technique (branched DNA) to measure the concentration of the virus. The measure of HCV RNA viral levels do not correlate with the severity of hepatitis as is the case when assessing HIV viral load. Rather, the quantification of HCV RNA in blood helps in predicting the likelihood of a response to antiviral therapy.[23] The amount of HCV RNA in the blood should therefore be assessed prior to the initiation of antiviral therapy in order to monitor treatment response. Since serial values are needed to monitor the antiviral therapy, it is recommended that the same quantitative assay be utilized for all assessments to reduce test variability.[8]

Recombinant Immunoblot

The strip immunoblot assay, also known as RIBA™, is a supplemental anti-HCV test manufactured by the Chiron Corporation (Emeryville, CA) with high specificity for four HCV-encoded antigens and synthetic HCV-encoded peptides immobilized as individual bands onto test strips. The two recombinant antigens (c33c and NS5) and two of the synthetic peptides (c100p and 5-1-1p) are derived from putative nonstructural regions of the virus, while the third peptide (c22p) corresponds to the putative nucleocapsid (core) viral protein.[26]

The recombinant immunoblot assay (RIBA) is useful in confirming the presence of HCV antibody when the EIA result is positive in the face of an undetectable HCV RNA.[27] A negative immunoblot result suggests that the positive HCV antibody test was a false positive result, whereas a positive immunoblot with two or more negative qualitative HCV RNA tests indicate that HCV infection has likely resolved. In both instances, no more further confirmatory HCV testing is needed.

HCV Genotyping

Since 80% of patients with HCV genotype 2 or 3 respond favorably to treatment, specialists do recommend that genotype testing be obtained in order to help make recommendations regarding therapy duration and likelihood of treatment response.[8] Genotype-specific antibodies can be assessed for the 6 genotypes by direct sequence analysis utilizing a technique of reverse hybridization to genotype-specific oligonucleotide probes or by the use of restriction fragment length polymorphism. These tests will not identify the genotype in less than 3% of HCV-infected individuals, and approximately 1%-4% of individuals may be identified to have a mixed genotype.[25]

Liver biopsy

The liver biopsy remains the only definitive test for the evaluation of liver fibrosis in HCV infected patients.[28] The CDC recommends that all co-infected patients who are candidates for antiviral therapy receive a liver biopsy unless contraindications are present.[8] The liver biopsy provides information regarding the degrees of fibrosis

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and hepatic inflammation. The Metavir scoring system and the Ishak grading system are scoring systems that characterize the amount of fibrosis (staging) and inflammation (grading). If the liver biopsy results demonstrate a Metavir score of ≥2 or an Ishak score of ≥3, treatment is recommended.[25] Studies have suggested that the degree of liver fibrosis is an independent predictor of treatment response.[25] Individuals with mild fibrosis generally have a better response to treatment than do patients with more severe fibrosis (bridging fibrosis or cirrhosis). The need for treatment, however, is stronger in the group with the more severe fibrosis.

In clinical practice, most specialists will obtain a liver biopsy for patients with HCV genotype-1 infection to help determine the need for treatment. It is argued that those with treatment responsive genotypes (2 or 3) should be treated regardless of the severity of liver disease and that a liver biopsy is not necessary to start treatment.[28] In patients who have been found to have little or no fibrosis on biopsy with a Metavir score ‹2 or Ishak score ‹3, liver biopsies can be obtained in intervals of 4 to 5 years to monitor the progression of liver disease.[25]

Generally, the extent of liver fibrosis correlates with elevated blood levels of aminotransferases. However, 14% to 24% of patients have normal aminotransferase levels despite having more-than-portal fibrosis on biopsy.[25] Cases such as these demonstrate the need for liver biopsy to facilitate treatment recommendations. The AASLD Practice Guidelines recommend that a liver biopsy be done regardless of aminotransferase blood levels, but a biopsy is not mandatory for the initiation of therapy.[25]

The problem with the liver biopsy is that it is invasive, expensive, and has complications. Complications include puncture of another organ, infection, bleeding (1/100 to 1/1,000 cases), and deaths (1/5,000 to 1/10,000 cases).[23] Higher rates of complications have been reported in HIV-co-infected patients with thrombocytopenia, coagulation defects, or liver lesions with high vascularity.[8] In these patients, it may be preferred to obtain a transjugular liver biopsy.[8]

Current investigations are looking at non-invasive markers of inflammation and fibrosis (such as serum fibrosis markers and tissue elastography), but their utility in HIV/HCV co-infected patients requires further validation studies.[8,25,28] These markers demonstrate utility in differentiating between low, intermediate, and advance grades of liver fibrosis but not between different levels of intermediate fibrosis scores.[29]

Further Evaluation

Biochemical markers are important components of initial and ongoing monitoring of HCV in HIV-infected persons. Increases in alanine (ALT) and aspartate (AST) aminotransferases range from 0 to 20 times (usually ‹5 times) the upper limit of normal with HCV infection.[23] In general, ALT is higher than AST in hepatitis C infection (approximately 10-fold elevation in acute hepatitis C infection), but may be reversed with cirrhosis. In approximately 5%-10% of cases, elevations in aminotransferases will occur with the initiation of antiretroviral therapy, which makes it more difficult to clearly delineate the etiology of the hepatotoxicity.[30] Certain subgroups will not demonstrate a rise in liver enzymes despite a persistent HCV RNA viremia.[19]

Further evaluation should include a complete blood count (CBC), hepatic panel, prothrombin time (PT), ferritin, thyroid stimulating hormone (TSH), and anti-nuclear antibody.[31] Alkaline phosphatase and gamma glutamyl transpeptidase levels are often normal; if elevated, they may be indicators of cirrhosis. Also with severe fibrosis or cirrhosis, rheumatoid factor may be present, and low platelet or white blood cell counts may occur. The prothrombin time and albumin levels are usually normal until advanced disease occurs. The LDH and creatine kinase are generally normal, while iron and ferritin levels may be slightly elevated. In 60% of cases, serum cryoglubulins are present but will rarely (‹5%) present symptomatic disease.[8] Further evaluation includes tests to screen for HCC using alfa-fetoprotein (AFP) and performing an ultrasound of the liver at 6-month intervals for co-infected patients with cirrhosis.[8]

Hepatitis C Treatment

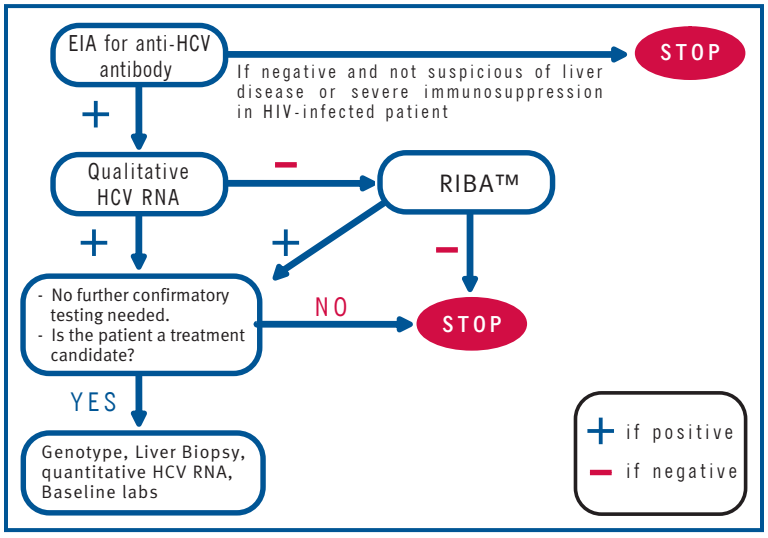
Who Should Be Treated?

All patients with chronic HCV infection should be considered for antiviral therapy.[8] Multiple factors must be considered in deciding whom to treat. These include genotype, degree of fibrosis, symptoms, need for or currently on HAART, age, severity of other underlying conditions, and patient motivation.[8] Patients with a detectable plasma HCV RNA on qualitative assay, histologic evidence of portal or bridging fibrosis with moderate to severe degrees of inflammation and necrosis, persistently elevated serum aminotransferase (ALT) levels (›2 times the upper limit of normal), and without contraindications are good candidates for antiviral therapy.[8,23]

Contraindications to Treatment

The following patients have contraindications to treatment: patients with clinically decompensated cirrhosis secondary to HCV (ascites, persistent jaundice, wasting, variceal hemorrhage, or hepatic encephalopathy), kidney/liver/heart/or other solid-organ transplant, and severe depression.[23] Contraindications to ribavirin include patients with unstable cardiopulmonary disease, erythropoietin-resistant anemia, and hemoglobinopathies. These patients, however, can take pegylated interferon-based monotherapy in absence of other contraindications.[8] Treatment of HCV with interferon (IFN) and/or ribavirin is contraindicated during pregnancy.[8] Women of childbearing age should agree to use contraception

Figure 1. Laboratory Testing for HCV in HIV-infected Patients



during treatment and for 6 months after its completion prior to the initiation of HCV treatment .[8]

Counseling and Prevention

Counseling all patients with chronic hepatitis C to avoid alcohol consumption is necessary due to the increased risk of fibrotic progression.[8,10,32] Co-infected patients are at increased risk of fulminant hepatic failure with the hepatitis A virus (HAV) and should be advised to take 2 doses of the HAV vaccine before the CD4+ count becomes ‹200 cells/µL as well as the hepatitis B (HBV) vaccine series.[8, 32]

Treatment Recommendations and Outcomes

Treatment recommendations for HCV/HIV co-infected patients remain complicated. The goal of antiviral therapy in co-infected patients is a sustained virologic response (SVR), which is defined as the absence of detectable HCV-RNA six months after the completion of treatment.[29] Approved antiviral therapies for patients with HCV mono-infection include monotherapy with standard interferons (alfa-2a, alfa-2b or IFN alfacon-1) or pegylated (PEG) interferons (alfa-2a or alfa-2b) and combination therapy with standard or PEG IFN plus ribavirin. In HCV mono-infected patients, sustained viral response has been observed in approximately 40% of patients with HCV genotype 1 and as high as 70% to 80% in patients with genotypes 2 or 3 with the pegylated interferon plus ribavirin combination, which is actually 7% to 12% higher than the standard IFN/ribavirin combination.[16]

Because data on the optimal duration of therapy for co-infected individuals is lacking, most clinicians utilize treatment recommendations for HCV mono-infected patients. For patients with HCV genotype 1 (estimated at 75% by the CDC) who have an EVR at 12 weeks of treatment, the CDC recommends a 48 week treatment duration with PEG IFN plus ribavirin. Patients who do not demonstrate an EVR at 12 weeks will not likely achieve an SVR regardless of treatment duration, and in such patients, it is recommended that treatment be stopped.[8,36] For patients with HCV genotypes 2 or 3, the recommended treatment duration is 24 weeks for co-infected individuals.[8,25] However, some specialists still recommend that the duration should extend to 48 weeks for co-infected patients.[8,29,36]

Four pivotal studies, the French Ribavic (ANRS HCO2) study, the Laguno et al. study (also known as the Laguno study), the AIDS Clinical Trials Group A5071 study (ACTG 5071), and the AIDS Pegasys Ribavirin International Co-infection Trial (APRICOT), have validated the efficacy of PEG IFN plus ribavirin combination therapy in HIV/HCV co-infected individuals.[33-36] The summary in Table 2 demonstrates that the SVR in co-infected patients on PEG IFN plus ribavirin have ranged from 27% to 44%.[33-36] These results may not be as high as the SVR in mono-infected individuals, but they do represent an improvement in SVR compared to the standard IFN/ribavirin combination in co-infected individuals. Response to treatment is more favorable in genotypes 2 or 3 as compared to genotype 1, and therefore, genotype remains a strong predictor of SVR. Other predictors of SVR in these studies included low HCV viral load for genotypes 1 and 4 (‹800,000 IU/ml), younger age, absence of cirrhosis, and ALT levels three times the upper limits of normal.[10,29]

The RIBAVIC, ACTG 5071, and APRICOT studies demonstrated that early virologic response (EVR), which is defined as an undetectable HCV RNA level (‹50 IU per ml) or a decrease of 2 $\log_{10}$ or more in the HCV viral load by week 12 of treatment, had a negative predictive value.[25,29-30] In this case, the studies found that patients who did not have an EVR at week 12 of treatment failed to achieve an SVR at week 72.[35-36] Chung et al. also found that in subjects who did not have virologic response to treatment, more than one-third did have histologic evidence of improvement based on liver biopsy.[35] Thus, the treatment combination appears to be beneficial for more than just the virologic response, and more studies are therefore needed to evaluate the treatment as maintenance therapy. It was also found that PEG IFN alfa-2a monotherapy was more effective than IFN alfa-2a plus ribavirin (SVR 20% vs. 12%, P=0.008), a finding that makes PEG IFN alone a better alternative for patients with ribavirin contraindications.[36]

Based on the results of these randomized, controlled trials, the CDC, NIH, and the HIV Medicine Association/IDSA recommend the use of PEG IFN alfa-2a 180 µg administered weekly by subcutaneous injection (or PEG IFN alfa-2b 1.5 µg/kg) plus oral ribavirin in a dose of 600-1,400mg/kg daily for chronic hepatitis C in patients co-infected with HIV (See Table 3).[8]

Response to HCV therapy may correlate to CD4+ T lymphocyte count. Patients with higher CD4+ cell counts (›500 cells/µL) have demonstrated more favorable response to treatment.[37] Furthermore, HAART appears to favorably affect the course of HCV by lowering liver-related morbidity and mortality in co-infected patients.[12] Thus, the CDC recommends that HCV treatment should be considered before the CD4+ T lymphocyte count falls below 500 cells/µL.[8,14] However, for HIV-infected patients who already have a CD4+ T lymphocyte count below 500, the recommendation is to initiate antiretroviral treatment prior to treating HCV.

Monitoring and Adverse Effects

The best monitor for treatment response at this time is the quantitative HCV RNA assay. The CDC's recommendations[8] for treatment monitoring of HCV in HIV-infected patients are the following:

- Quantitative HCV RNA assay should be done at the end of weeks 12 and 24 of treatment.
- Patients with undetectable HCV RNA levels should have a repeat HCV RNA assay at 24 weeks after treatment completion.
- Patients who do achieve a SVR should have HCV RNA levels repeated at 6 month intervals for 1-2 years to exclude late virologic relapse or re-infection (for patients with continued exposure risk).

Relapse is defined as the absence of detectable HCV RNA at the end of treatment (ETR) that is not sustained over time, and nonresponse is the absence of ETR or SVR.[8] For non–responders with minimal disease, it is better to wait before restarting therapy, but for non-responders with more advanced disease, re-treatment is the option of choice.[29]

Re-treatment decisions should be based on type of previous treatment, type of response or non-response, tolerability to previous therapy, extent of liver damage, and HCV genotype.[8,10] Strategies for re-treatment include high-dose induction of PEG IFN/ribavirin

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Table 2. Four Trials Comparing Pegylated Interferons Plus Ribavirin to Standard Interferon Plus Ribavirin Therapy for Hepatitis C in HIV Co-Infected Patients

Study	RIBAVIC[33]	Laguno Study[34]	ACTG 5071 [35]	APRICOT[36]
Setting	France	Spain	U.S.A.	International
Design	Multicenter, randomized, controlled, open-label trial	Single center, randomized, open-label trial	Multicenter, randomized, controlled, open-label trial	Multicenter, randomized, controlled trial
Patients	412	95	133	868
Intervention	**Ribavirin** 800mg/day plus either **PEG IFN alfa-2b** 1.5µg/kg/week or **standard IFN alfa-2b** 3 MIU three times/week	**Ribavirin** 800-1200 mg/day (depending on body weight) plus either **PEG IFN** alfa-2b 1.5µg/kg/week or **standard IFN alfa-2b** 3 MIU three times/week	**Ribavirin** escalating doses starting at 600mg/day X 4 weeks, 800mg/day X 4 weeks to a maximum of 1000 mg/day plus either **PEG IFN** alfa-2a 180µg/week or **standard IFN alfa-2a** 6 MIU three times/week X 12 weeks, then 3 MIU three times/ week X 36 weeks	**PEG IFN** alfa-2a 180 µg/week plus either **Ribavirin** 800mg/day or Placebo or **standard IFN alfa-2a** 3 MIU three times/week plus **Ribavirin** 800mg/day
Duration of Treatment	48 weeks	48 weeks (genotype 1) 24 weeks (genotypes 2 or 3 plus low viral load)	48 weeks	48 weeks
Treatment Effectiveness: Sustained Virologic Response (SVR) **PEG IFN/Ribavirin vs. Std IFN/Ribavirin**	27% vs. 20% *(P=0.047)*	44% vs. 21% *(P=0.017)*	27% vs. 12% *(P=0.03)*	40% vs. 12% *(P<0.001)* PEG IFN/Ribavirin vs. Placebo 40% vs. 20% *(P<0.001)*
SVR by genotype 1 (or 4) **2 or 3 (or 5)**	17% vs. 6% *(P=0.006)* 44% vs. 43% *(P=0.88)*	38% vs. 7% *(P=0.007)* 53% vs. 47% *(P=0.730)*	14% vs. 6% (No P value given) 73% vs. 33% *(P=0.07)*	29% vs. 7% vs. 14% (placebo)-No P value given 62% vs. 20% vs. 36% (placebo)-No P value given

combination and long-term maintenance therapy with PEG IFN to delay or prevent liver disease progression.[29] Relapse rates in all of the co-infection treatment trials were significant (approximately 20%).[29,36] For treatment relapsers, studies are being conducted to examine increasing duration of treatment, higher ribavirin dosing, and newer therapies.[29]

Toxicities to interferon alfa commonly include influenza-like symptoms (fever, myalgia, HA, and fatigue) and problems with depression.[8] These symptoms occurred in 20%-45% of patients in all four PEG IFN studies.[29] Depression may be severe enough to lead to suicide and peaks around the 4th month of treatment.[8,29] Cytopenias (thrombocytopenia, neutropenia, decrease in CD4+ cell count) are also common complications of IFN therapy. Neutropenia has been documented in 50% patients receiving the PEG IFN/ribavirin combination.[29] Other complications include retinopathy, neuropathy, exacerbation of autoimmune disease, and weight loss.

Ribavirin toxicities include a dose dependent hemolytic anemia, cough, and dyspepsia. The occurrence of drug-drug interactions between ribavirin and anti-HIV pyrimidine nucleoside analogues (ZDV, stavudine, zalcitabine, and lamivudine) have been concerning and warrant closer monitoring of patients who are on these antiretroviral therapies.[8] Furthermore, interactions between ribavirin and didanosine have led to the inhibition of mitochondrial DNA and have been significant enough to cause severe pancreatitis and lactic acidosis.[33-34] Therefore, the combination of ribavirin and didanosine is contraindicated currently.[8] Furthermore, the APRICOT study found a reduction in the total number of CD4+ cells but an increase in the percentage; however, during the study follow-up, the cell counts returned to pretreatment levels.[29,36]

Some of these complications of therapy may be treated with agents such as NSAIDS (flu-like symptoms), antidepressants, filgrastin (neutropenia), and erythropoietin (anemia).[8,29,34] Although G-CSF has been utilized for the treatment of neutropenia, there have been no randomized trials to confirm the efficacy of this treatment in co-infected patients.[29] Because of the multitude of adverse effects that may occur with HCV treatment, the CDC recommends that ongoing monitoring and laboratory evaluation occur. Baseline CBC, HCV RNA viral load, CD4+ T lymphocyte count, and mental health evaluations should be checked before initiation of and during treatment.

Conclusion

HIV/HCV co-infection is a significant problem, but as the four major trials suggest, treatment of HCV with pegylated interferon alfa plus ribavirin is relatively safe and effective in HIV-infected patients. This combination is now the standard of care. Newer studies are needed to evaluate the duration of therapy, to examine the dosage of ribavirin treatment, to determine the role of maintenance therapy, and to find effective management strategies for non-responders and relapsers. Because the efficacy of the PEG IFN/ ribavirin combination is lower in co-infected patients with HCV

Table 3. Treatment Algorithm of HCV in Co-Infected Patients

Genotype	Treatment	Alternative Therapy	Treatment Duration	Treatment Monitoring
1	Peginterferon alfa-2a 180 µg SQ weekly or Peginterferon alfa-2b 1.5 µg /kg SQ weekly and Ribavirin PO (weight-based) If ‹75kg (165 lbs), 400mg in am and 600 mg in pm If ›75kg, 600 mg BID	Patients with ribavirin contraindication*: Peginterferon alfa-2a 180 µg SQ weekly or Peginterferon alfa-2b 1.5 µg /kg SQ weekly	48 weeks—for patients who demonstrate an EVR,** (monitor symptoms, blood counts, and ALT at 4- to 8-week intervals) 12 weeks—for patients who failed to achieve an EVR at 12 weeks***	After therapy, assess aminotransferases at 2- to 6-month intervals. In responders, repeat HCV RNA testing 6 months after stopping.
2 or 3			24 weeks—based on data in non-HIV-1-infected patients; some specialists recommend 48 weeks	

NOTE. Table adapted from Centers for Disease Control and Prevention. Treating opportunistic infections among HIV-infected adults and adolescents. MMWR. 2004;53(RR-15):49-53,100.

*e.g. unstable cardiopulmonary disease, pre-existing anemia or hemoglobinopathy
**≥2 log decrease in HCV viral load at 12 weeks
*** therapy beyond 12 weeks is almost always futile for achieving virologic cure

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genotype 1, HCV liver-related morbidity and mortality will continue to trouble co-infected patients until newer therapies are found. Studies to definitively answer the role of liver biopsy and evaluate the newer liver markers are also needed. A comparison study of the pegylated interferons in co-infected patients is warranted. The future of HIV/HCV co-infection treatment remains an avenue where improvements in HCV therapy can significantly impact the lives of patients burdened by these diseases.

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HIV and Hepatitis C Case Discussion

Contributed by Shobha Swaminathan, MD
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The Infectious Diseases Practice at the University Hospital of UMDNJ, Newark serves about 1,200 patients infected with HIV. Of these, about 40% are coinfected with HCV, at least 70% of whom have genotype 1. In order to effectively manage this coinfection, the clinic team developed an integrated team model that includes:

1) HIV physician
2) Hepatologist
3) Nurse clinician
4) Mental health counselor
5) Nutritionist

All the above personnel are located on-site in the clinic making it more accessible for patients. Patients with HIV-HCV are referred by their primary physician to the hepatologist to determine eligibility for treatment. The mental health counselor and the nutritionist then evaluate all eligible candidates. This is critical to the success of treatment because depression, at times with suicidal ideation, has been reported in patients undergoing treatment for HCV. Based on the mental health counselor's evaluation, patients with elevated risk for depression are referred to a psychiatrist for assessment and treatment, which may include anti-depressant medication and/ or ongoing therapy. The final decision to initiate HCV treatment is made by the team. The nurse clinician works closely with the patient, the HIV physician and the hepatologist and helps to coordinate their care. The nurse is not only responsible for education about the disease, medications, and injection techniques but also functions as an adherence counselor throughout the course of treatment. The team follows patients very closely to ensure that toxicities of treatment, if any, are identified and managed early on.

1) A 39-year old white male with HIV, with HCV Genotype 1 has CD4 426, VL ‹50 on Combivir® and lopinavir and ritonavir. He was started on therapy with pegylated interferon weekly and 1200 mg of ribavirin daily. His baseline labs revealed a hemoglobin of 11.0g/dl, AST-63 U/dl and ALT-72. He came in to the clinic 6 weeks later with severe fatigue and inability to function. He was found to be severely anemic with a Hb 6.0 g/dl.

What would you do next?

a) Transfuse with packed red cells and discontinue HCV therapy.
b) Discontinue HCV therapy.
c) Start patient on erythropoeitin alone.
d) Continue current management.

Answer: a. This patient already had some baseline anemia to begin with, which may have been as a result of chronic HIV infection or as a result of being on zidovudine. The addition of ribavirin to the regimen probably caused hemolysis thereby worsening his anemia. As an outpatient his HAART regimen was initially changed to Epzicom TM (abacavir sulfate and lamivudine) and Kaletra® (lopinavir/ritonavir), and his hemoglobin remained at 11.5 g/dl with all other work up for anemia being negative. The patient was however very motivated, and wanted to restart his HCV treatment; hence he was started on weekly pegylated interferon with a slightly lower dose of ribavirin of 1000 mg. He was closely monitored with weekly CBC and was also started concurrently on erythropoietin weekly injections. He continues to do well and is at 12 weeks now. By giving erythropoietin we were able to maintain his HCV treatment with ribavirin on board thus improving his chance for effective HCV viral load suppression.

2) A 47-year-old Black male with HIV/HCV, CD4 202, and VL 150,000 came in asking why he was not being treated for HCV. He only occasionally has a drink, and has a history of depression which seems to be currently controlled. His baseline labs show HCV PCR- › 7,700,000 IU/mL and HCV genotype 1b. He is taking Epzicom, Viread® (tenofovir disoproxil fumarate), Reyetaz® (atazanavir sulfate) and Norvir® (ritonavir).

You will:

a) Discuss the need to get his HIV under control first.
b) Encourage total abstinence from alcohol.
c) Encourage patient to be seen by a psychiatrist.
d) All of the above and discuss further testing before treatment.

Answer: d. This patient had several relative contraindications to treatment. His HIV was poorly controlled with a relatively low CD4 count and he continues to drink alcohol. All of these may indicate a relatively non compliant patient who would run a higher risk of complications with HCV therapy. In addition, he would benefit from close psychiatric follow up to ensure that his depression stays well controlled.

3) A 36-year old white male with HIV and HCV has an HIV VL‹50, CD4 of 424. His HCV VL is ›1 million copies/ml with genotype 1b. His current medications include Videx® (didanosine, or ddI), Epivir® (lamivudine or 3TC), and Kaletra, and his liver biopsy reveals some areas of fibrosis.

What will you do next?

a) Start him on interferon and ribavirin.
b) Change Videx to Viread.
c) Change Kaletra to Reyataz.
d) Tell him that he can wait for a few years before getting HCV treatment.

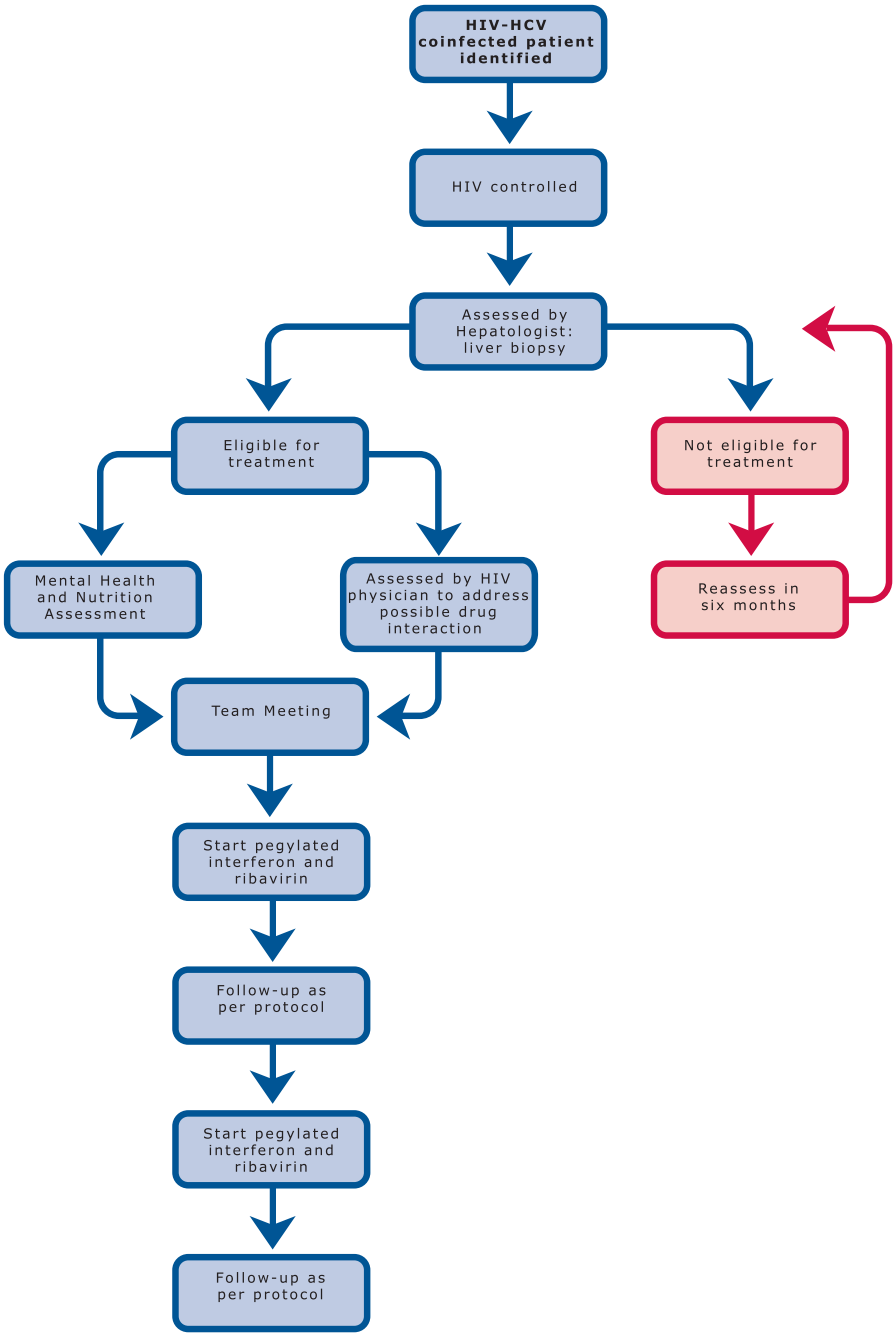
Answer: b. There are many drug interactions between HIV medications and HCV treatment. Videx is contraindicated in patients undergoing HCV treatment due to the risk of severe hepatotoxicity. Hence these patients must always be managed by a team of professionals who understand the intricacies of this patient population. The patient's regimen was changed to Truvada and Kaletra, and the patient did well.

4) A 51-year old Black male with HIV, CD4 556, VL 431 on Combivir, Viread, Reyataz and Norvir, has an HCV PCR › 3,000,000, and HCV Genotype 1. Labs reveal a serum albumin- 2.3, bilirubin- 3.0, ascites- +, encephalopathy +, INR- 1.3, platelet count of 35,000/ml.

What do you do next?

a) Tell the patient that he needs to be started urgently on HCV treatment because of his advanced liver disease.
b) Discuss with the patient the risks of HCV treatment including liver failure, bleeding.
c) Tell him that you need a liver biopsy before you can discuss treatment options with him.
d) Tell him that because his HIV is well controlled, he should do well with HCV treatment.

Answer: b. This type of presentation is becoming increasingly prevalent in the HIV clinic. This patient clinically has evidence of advanced liver cirrhosis with evidence of liver failure. He would have a very high rate of complication with treatment using standard pegylated interferon and ribavirin. The clinician should inform him of the risks, and if he chooses to receive treatment, he should be referred to a tertiary center for evaluation by a specialist.



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Hepatitis C and HIV Resources and Information

HIV and Hepatitis.com

http://hivandhepatitis.com

This website provides summaries of key news articles and conference reports, updates on new Anti-HCV Therapies in Development, and treatment summaries for both clinicians and consumers

Notable quote:

"Despite the improvement in hepatitis C therapy offered by the pegylated interferons Pegasys and PegIntron, more than half of individuals with chronic hepatitis C do not achieve a sustained response from these treatments, which also are relatively expensive and may produce serious or even life-threatening adverse events. In addition, certain patient groups experience consistently inferior virological responses to combination treatment with interferon and ribavirin, including African Americans, persons with genotypes 1 and 4 and HIV-HCV coinfected individuals."

Ronald Baker, PhD, *publisher and editor in chief of HIV and Hepatitis.com*

CDC Viral Hepatitis webpage

Hepatitis A, B and C Resource Center:

http://www.cdc.gov/ncidod/diseases/hepatitis/

Free patient and provider materials including pamphlets and slide sets, surveillance guidelines and reports, and frequently asked questions

http://www.cdc.gov/ncidod/diseases/hepatitis/resource/index.htm

Syringe Disinfection for Injection Drug Users

"The central message is that disinfection is a back-up prevention strategy if the user cannot stop injecting; does not have a new, sterile syringe; and is about to inject with a syringe that has been used before."

http://www.cdc.gov/idu/facts/disinfection.htm

The Ribavirin Pregnancy Registry

This is a voluntary Registry established to collect and evaluate pregnancy exposures to ribavirin, and assess any birth defects occurring in outcomes of pregnancy exposed to ribavirin in-utero. Pregnancy exposures to ribavirin include those occurring during pregnancy or up to six (6) months before conception, and indirect exposures through a male sexual partner who has taken ribavirin.

Toll-Free: (phone) 800-593-2214 (fax) 800-800-1052
E-Mail: registry@nc.crl.com

http://www.ribavirinpregnancyregistry.com

AIDS InfoNet

The AIDS InfoNet is a project of the New Mexico AIDS Education and Training Center in the Infectious Diseases Division of the University of New Mexico School of Medicine. The InfoNet was originally designed to make information on HIV/AIDS services and treatments easily accessible in both English and Spanish for residents of New Mexico, and has become an international HIV/AIDS information resource. www.aidsinfonet.org

Fact Sheet Number 507: Hepatitis C and HIV:

http://www.aidsinfonet.org/articles.php?articleID=507

Notable quote:

"Almost all cases of hepatitis C could be cured if treatment with interferon starts very soon after infection. Unfortunately, early signs of hepatitis can seem like the flu. Most cases are not diagnosed until years after infection."

NATAP: National AIDS Treatment Advocacy Project

http://natap.org

- The **NATAP Reports** newsletter
- The **Women's Program:** Provides Women specific treatment information
- **Daily Worldwide E-mail Treatment Updates** on both HIV & HCV
- **NATAP Community Treatment Education Program**: on-site education in English and Spanish for community based organizations.
- Additional periodicals & printed brochures: **"The Hepatitis C and Hepatitis C-HIV Co-Infection Handbook"** (In English & Spanish), "What you need to know about HIV/HCV coinfection"and Fact Sheets are available free on website.

Hepatitis C in New Jersey:

New Jersey Strategic Plan for Hepatitis C Prevention And Control [January 2005]

http://www.state.nj.us/health/cd/hepatitisc_strategic_plan.pdf

"CDC estimates that 1.8% of Americans are infected with HCV, the most common bloodborne infection in the United States today. In New Jersey, 1.8% would translate to roughly 155,000 infected persons. However, these statistics probably do not adequately reflect the full extent of the problem. Hepatitis C has been a reportable disease in New Jersey since 1998, and the number of reported cases has increased annually. **In 2003 in New Jersey, there were 3,300 reported cases of newly diagnosed hepatitis C.** There were 2,200 cases reported in 2002. However, it is estimated that New Jersey's true incidence of hepatitis C is grossly underreported and underdiagnosed. Information on race, risk factor, ethnicity, comorbidity and treatment data are lacking for most of our reported cases."

Patient Assistance Programs for HCV Therapy from Drug Manufacturers: Pegylated Interferon and ribavirin

If you cannot get reimbursement or coverage for pegylated interferon and ribavirin, the manufacturers have reimbursement programs which supply free drugs if you qualify. These programs will first help you try to identify sources for reimbursement.

- Schering makes Peg-Intron and ribavirin (Rebetol):

1-800-521-7157

http://www.peg-intron.com

- Roche makes Pegasys and ribavirin (Copegus):

1-800-387-1258

http://rocheusa.com/programs/patientassist.asp

NJ Physicians Treating Hepatitis

Hepatitis-Central:
http://hepatitis-central.com/hcv/drs/nj/toc.html

HIV/AIDS Medical Update Series: Healthcare Provider Training

To schedule a free 1-hour HIV medical education program at your health care site on HIV/AIDS and Hepatitis C Co-Infection or any of the other topics in the HIV/AIDS Medical Update Series, contact Debra Bottinick at (609) 921-6622 or dbottinick@academycme.org. See page 20 for more information about this series

Hepatitis C Harm Reduction Project

A Resource for Drug Users sponsored by the Harm Reduction Coalition: fact sheets, blogs, tips

http://hepcproject.typepad.com/hep_c_project

Treatment from a Consumer and Treatment Advocate's Perspective*

Advice from an interview with a long-time treatment advocate, educator, and outspoken consumer of HIV and Hepatitis C treatment:

- Learn about your liver, and the stage of your hepatitis. Read about it, talk to your doctor, talk to other people who are co-infected and have been on treatment.
- Weigh treatment of your Hepatitis C and its side effects against the severity of its current stage: can I wait till better treatment comes along, or do I need to be pro-active and keep my liver disease from progressing?
- Get your HIV under good control first, unless your liver is in danger.
- Get support before you begin treatment, and plan how you will manage this complex regimen, remembering:
  - o You need a support system: friends, family, religious leader or community, medical team, life partner, support group.
  - o You may have low energy and poor appetite: ask friends and family to help with prepared food, check-in calls.
  - o Many physicians managing HIV and HCV choose to prescribe anti-depressants before beginning HCV treatment, to ward off depression before it can become serious. If you have any concerns about your mental health, especially if you've ever been depressed, be sure to talk about it with your doctor and the treatment team, and get into treatment before you start Hep C treatment.
  - o Drink lots of water! And remember to eat even if you don't feel hungry.
  - o Write down everything: lab tests, treatment options, prescriptions and directions, symptoms including mood changes.
  - o Know whether injecting yourself 1-3 times a week will be a relapse trigger: if you used to inject drugs, you may need to get some extra support for staying clean and sober.

"Why did I decide to start treatment? I wanted to preserve my liver and contain the damage. I knew I was filtering a lot of HIV meds through my liver and I knew I would benefit from hepatitis treatment. The first time, it didn't work. I was devastated because I was doing everything I was supposed to do. But when the next treatment came along (pegylated interferon & ribavarin), I decided to start again, and this time I had more side effects, but the treatment started to show in my test results. I weighed the difficulties of the treatment against the benefit: on the one hand, if I stick with all the shots and pills, I might feel lousy for a while, lose some hair and weight … or on the other hand I may have my liver fail, and die. Which one do I want? That made it easy. I had hope the whole time, and that kept me going. Even if I hadn't gotten to an undetectable viral load, at least my liver would be in better shape and I would live longer."

**** Thanks to Yolonda, a great consumer educator and advocate!***

CME

CME QUIZ

Update on HIV and Hepatitis C Virus Co-Infection

Questions refer to the content of the article and the notes that follow. To receive CME credit: complete exam, registration, and evaluation forms on-line at http://ccoe.umdnj.edu/aids or fill in the forms on the next 2 pages, and mail or fax to UMDNJ-CCOE (see next page).

CME

1. Which of the following is the estimated prevalence of HIV/HCV co-infection among all HIV-positive people in the U.S.?

   a. ‹5%
   b. 5%-10%
   c. 15%-25%
   d. ›40%

2. At this time, what is the most common route of HCV transmission?

   a. Injection drug use
   b. Needle stick injuries
   c. Sexual
   d. Vertical

3. Patients with HIV/HCV co-infection have:

   a. A lower number of hepatitis-related deaths than patients with HCV mono-infection
   b. Decrease in CD4+ cell count when they initiate HAART as compared to patients with HIV mono-infection
   c. Slower progression to cirrhosis and hepatocellular carcinoma than do patients with HCV mono-infection
   d. Higher blood levels of HCV RNA as compared to patients with HCV mono-infection

4. AASLD guidelines recommend HCV testing for which of the following individuals?

   a. Health care workers
   b. Patients with hemophilia
   c. Patients with HIV infection
   d. Patients who received a transfusion of blood or blood products in 2002

5. Which of the following is the recommended laboratory protocol for the diagnosis of HCV infection?

   a. EIA→RIBA
   b. EIA→qualitative HCV RNA assay→RIBA
   c. Quantitative HCV RNA assay→RIBA
   d. RIBA→qualitative HCV RNA assay→quantitative HCV RNA assay

6. Liver biopsies should be done in which of the following patients?

   a. All co-infected patients
   b. Patients with abnormal serum liver enzymes only
   c. Patients with genotype 1 only
   d. Patients with genotype 2 or 3 only

7. Which of the following is a contraindication for pegylated interferon?

   a. Hepatitis B infection
   b. HIV infection
   c. Pregnancy
   d. Renal disease

8. What is the CDC recommended treatment duration for patients who are co-infected with HIV and HCV?

   a. PEG IFN/ribavirin combination therapy for 24 weeks for genotypes 1,2,3
   b. PEG IFN/ribavirin combination therapy for 48 weeks for genotypes 1,2,3
   c. PEG IFN/ribavirin combination therapy for 48 weeks for genotype 1 and 24 weeks for genotypes 2 or 3
   d. PEG IFN/ribavirin combination therapy until SVR achieved

9. At what point during therapy should HCV RNA be re-evaluated?

   a. 12 weeks
   b. 24 weeks
   c. 12 and 24 weeks
   d. 48 weeks

10. Which of the following drug-drug combinations is currently contraindicated with PEG IFN/ribavirin therapy?

    a. PEG IFN and stavudine
    b. PEG IFN and zidovudine
    c. Ribavirin and didanosine
    d. Ribavirin and lamivudine

University of Medicine and Dentistry of New Jersey
Center for Continuing and Outreach Education

Update on HIV and Hepatitis C Virus Co-Infection

Registration Form

In order to obtain AMA PRA category 1 credit, participants are required to:

(1) Read the learning objectives, and review the activity, and complete the self-assessment.

(2) Complete this registration form and the activity evaluation form on the reverse side, and record your test answers below

(3) Send the registration and evaluation forms to:

UMDNJ-Center for Continuing and Outreach Education

via mail: PO Box 1709, Newark, NJ 07101-1709

via fax: (973) 972-7128

(4) Retain a copy of your test answers. Your answer sheet will be graded and if a passing score of 70% or more is achieved, a CME credit letter awarding AMA/PRA category 1 credit and the test answer key will be mailed to you within four (4) weeks. Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again.

Individuals who fail to attain a passing score will be notified and offered the opportunity to complete the activity again. This activity will be posted online at http://ccoe.umdnj.edu/aids

Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of completed evaluation form.

SELF-ASSESSMENT TEST

Circle the best answer for each question on page 10.

1. A B C D
2. A B C D
3. A B C D
4. A B C D
5. A B C D
6. A B C D
7. A B C D
8. A B C D
9. A B C D
10. A B C D

Registration

First Name_____M.I._____ Last Name_____Degree_____

Daytime Phone # _____ Evening Phone #_____

Fax #_____ E-mail_____

Preferred Mailing Address: ____Home ____Business

Address_____

City_____State_____Zip Code_____

Affiliation, Specialty_____

I attest that I have completed the activity as designed and I am claiming [up to 1 credit] _____ AMA/PRA category 1 credit

Signature_____ Date_____

Credit for this activity is available until December 31, 2006

UMDNJ-Center for Continuing and Outreach Education
PO Box 1709, Newark, NJ 07101-1709
Phone: 973-972-4267 or 1-800-227-4852
Fax: 973-972-7128

CE Activity Code: 07HC08-DE01

CME

University of Medicine and Dentistry of New Jersey
Center for Continuing and Outreach Education

Update on HIV and Hepatitis C Virus Co-Infection

Activity Evaluation Form

The planning and execution of useful and educationally sound continuing education activities are guided in large part by input from participants. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few moments to complete this evaluation form. Your response will help ensure that future programs are informative and meet the educational needs of all participants. Please note: CE credit letters and long-term credit retention information will only be issued upon receipt of this completed evaluation form. Thank you for your cooperation!

PROGRAM OBJECTIVES: Having completed this activity, are you better able to:	Strongly Agree				Strongly Disagree
Objective 1: To describe the epidemiology and natural history of HIV/HCV co-infection.	5	4	3	2	1
Objective 2: To recognize the role of laboratory testing for the diagnosis and ongoing monitoring of HCV in HIV-infected patients.	5	4	3	2	1
Objective 3: To identify HCV treatment candidates and implement evidence-based treatment regimens for the management of HCV in HIV co-infected patients.	5	4	3	2	1

OVERALL EVALUATION:	Strongly Agree				Strongly Disagree
The information presented increased my awareness/understanding of the subject.	5	4	3	2	1
The information presented will influence how I practice.	5	4	3	2	1
The information presented will help me improve patient care.	5	4	3	2	1
The faculty demonstrated current knowledge of the subject.	5	4	3	2	1
The program was educationally sound and scientifically balanced.	5	4	3	2	1
The program avoided commercial bias or influence.	5	4	3	2	1
Overall, the program met my expectations.	5	4	3	2	1
I would recommend this program to my colleagues.	5	4	3	2	1

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so.

_____

_____

_____

_____

Please provide any additional comments pertaining to this activity (positives and negatives) and suggestions for improvement. Please list any topics that you would like to be addressed in future educational activities:

_____

_____

_____

_____

CE Activity Code: 07HC08-DE01

In the News!

NJ Perinatal HIV Prevention Conference a Big Success

Perinatal HIV Prevention Poster Session

On November 3, 2005 the UMDNJ-Center for Continuing and Outreach Education, in collaboration with the New York/New Jersey AIDS Education and Training Center, the New Jersey Ryan White Title IV HIV Family-Centered Care Network, and the New Jersey Department of Health and Senior Services-Division of HIV/AIDS Services held a full-day symposium, "Reducing Perinatal HIV Transmission in New Jersey." The program was held at the NJ Hospital Association Conference Center and had 126 attendees, which included 75 clinicians. This conference was a great success, highlighting changes in clinical and public health protocols that have contributed to significant reductions in perinatal HIV transmission. The seminar also included a poster session made up of six posters that presented methods currently used to promote prevention of perinatal HIV transmission within New Jersey.

CDC HIV/STD/TB Prevention News Update 11/01/2005

UNITED STATES: "Food and Drug Administration Approves Tablet Form of HIV Inhibitor Kaletra"
Wall Street Journal (11.01.05): Dow Jones Newswires

Illinois-based Abbott Laboratories said it has received Food and Drug Administration approval for a tablet form of its HIV inhibitor Kaletra. The new form will allow adult patients to take fewer pills with or without food as part of their treatment regime, and it does not require refrigeration. These benefits are not available with the capsule form of Kaletra, which was introduced in 2000. According to pharmacokinetic studies in 141 non-HIV-infected healthy participants, Kaletra in the tablet form provided similar drug levels in the blood when compared to the capsule form.

Hotlines

National HIV/AIDS Clinicians' Consultation Center Expands Hotlines

The National HIV Telephone Consultation Service is a warmline available through NCCC from 8AM to 8PM EST Monday through Friday. It provides consultation for questions on HIV/AIDS, including antiretroviral therapy, antiretroviral drug resistance, opportunistic infection prophylaxis and treatment, and laboratory evaluation.

Warmline: 800-933-3413.

A new national resource, the **National Perinatal HIV Consultation and Referral Service**, is available for 24-hour consultation on preventing perinatal transmission of HIV from mother to infant. The consultation focuses on the management of HIV-infected pregnant women and exposed infants as well as indications and interpretations of rapid HIV testing in pregnancy. The perinatal hotline is part of the National HIV/AIDS Clinicians' Consultation Center (NCCC) of the University of California San Francisco at San Francisco General Hospital.

Perinatal hotline: 888-448-8765 (888-HIV-8765)

NCCC also offers consultation services for occupational exposures to blood-borne pathogens, 24 hours a day!

National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline): 888-448-4911 (888-HIV-4911)

CDC-INFO

For assistance concerning personal health issues, including questions regarding personal risk or where to get an HIV test, 24 hours, contact:

1-800-CDC-INFO (1-800-232-4636) TTY: 1-888-232-6348

For assistance concerning HIV/AIDS treatment, clinical trials, or vaccines, Monday-Friday, 12 – 5 PM, contact:

AIDSInfo:
1-800-HIV-0440 (1-800-448-0440) TTY: 1-301-519-0459 FAX: 1-301-519-6616

Continued from Page 1

Breakout workshop facilitators pointed us to a valuable web resource for substance abuse treatment through the NJ Department of Human Services, Division of Addiction Services (http://samsdev.rutgers.edu/dastxdirectory/txdirmain.htm), and the Mental Health Association of New Jersey's helpline, 866-202-HELP, or website (http://www.njmentalhealthcares.org). As the planning committee searched for speakers with the ability to uncover new or difficult to find resources for supportive services, we heard over and over again, "I can't find enough resources for my clients without HIV, let alone for those living with the virus!" Yes, there are ways to support clients in obtaining the necessities of daily living that are a barrier to their obtaining good quality healthcare and enjoying a healthier life with HIV. However, there is no silver bullet. As we try to make lemonade out of the lemons we have, we are beginning to be concerned that there are not even enough lemons to go around.

The Institute of Medicine reported in its May 2004 publication, entitled *Public Financing and Delivery of HIV/AIDS Care*, that 69% of the people living with HIV in the United States are not privately insured. These individuals access healthcare through a patchwork of federal and state funded programs, with 20% completely uncovered and dependent on CARE Act resources. Receiving adequate healthcare and medicines can be a challenge for CARE Act dependent clients in many states, while obtaining necessary support services may be next to impossible. The report goes on to explain that the level and quality of services varies significantly from state to state, and within states, there can be tremendous disparities based on the level of funding and the programs funded. Redirecting support service funding to clients with HIV who may previously have had CARE Act funded services will only slice the non-HIV specific resource pie into even smaller pieces. This is the sad reality that we face each day, even in one of the wealthiest states in the nation. New Jersey has one of the best publicly financed health care programs for persons living with HIV in the nation (e.g. our AIDS Drug Distribution Program has an open formulary and serves clients at up to 450% of the federal poverty level. We have six Eligible Metropolitan Areas serving clients with services throughout the state and 11 Title III funded healthcare centers, etc.). With all of the challenges our providers face in helping their clients access support services, one can only imagine the challenges faced by our colleagues and their clients in the Gulf Coast region.

Sending a message back to the Statewide Coordinated Statement of Need:

The conference featured 7 separate discussion groups divided by the Titles and programs of the CARE Act, and included a consumer needs group. The transcripts of these sessions are, at the time I write this, informing the Statewide Coordinated Statement of Need document for 2006. Emerging from these sessions were some common themes of need:

1. Resources must be streamlined and duplication must be eliminated: it is clearer than ever that no waste can be tolerated.
2. Consumers and providers need assistance in finding resources: creating systems and databases that link people with services is a vital investment in a future with no additional funding.
3. The Titles must work together in order to achieve any of their individual goals.

The highlight of the conference for most of the participants, based on the evaluations, was the keynote speech given by Christine Lubinski, MA, the Executive Director of the HIV Medicine Association. Ms. Lubinski provided a provocative overview of the state of the still-to-be-reauthorized CARE Act from a 30,000-foot perspective. Many of us were able to step back, be grateful for what we have, and consider that it is not helpful for us to fight over shrinking resources, when the same energy can be directed to more efficiently using what we have and articulating the very real need for more. We cannot genuinely help our own at the expense of others.

The Division is grateful to the conference participants and supporters, including the NJDHSS, Hyacinth AIDS Foundation and Rutgers University for the opportunity to host this vital discussion.

Dion Richetti, DC, is the Director of the Division of AIDS Education at UMDNJ – Center for Continuing and Outreach Education, and the co-chairperson of the NJ Statewide Coordinated Statement of Need Planning Task Force.

Internet Resources

HIV/AIDS Information and Guidelines

NJ Department of Health & Senior Services Division of HIV/AIDS Services (DHAS)

www.state.nj.us/health/aids/aidsprv.htm

Epidemiological reports, policies, and clinical guidelines for HIV/AIDS care and services in New Jersey. New Jersey HIV/AIDS Semi-annual Newsletter (statistical report)

http://www.state.nj.us/health/aids/aidsqtr.htm

New Jersey rapid testing site: FAQS, locations, and articles.

www.state.nj.us/health/aids/rapidtesting/index.shtml

US Dept. of Health & Human Services

www.aidsinfo.nih.gov

A service of the US Department of Health and Human Services offering HIV/AIDS treatment guidelines, other information on prevention, treatment, and research. National Institutes of Health-sponsored searchable database of clinical trials:

http://clinicaltrials.gov

Centers for Disease Control (CDC) Division of HIV/AIDS Prevention

HIV/AIDS research, surveillance reports [2004 summary now available], funding announcements, research and reporting software, surveillance/ epidemiology slide sets.

http://www.cdc.gov/hiv/hivinfo.htm#WWW

Rapid Testing Web page:

http://www.cdc.gov/hiv/rapid_testing

MMWR [Morbidity and Mortality Weekly reports]:

http://www.cdc.gov/hiv/pubs/mmwr.htm

CDC National Prevention Information Network (NPIN)

HIV, STD, and TB-related news summaries, funding announcements, materials, conference and satellite broadcast announcements.

http://www.cdcnpin.org

FDA MedWatch

Updated reports on medication interactions and warnings: 1-800-FDA-1088. Subscribe to e-bulletin:

http://www.fda.gov/medwatch/elist.htm

HIV/AIDS Training and Education

University of Medicine & Dentistry of NJ Center for Continuing and Outreach Education Division of AIDS Education

http://ccoe.umdnj.edu/aids

Training programs for HIV/AIDS health and social service professionals. You can register online for most UMDNJ HIV/AIDS continuing education courses at:

www.peopleware.net/0646a

Free online CME:

- Opportunistic Infections in HIV/AIDS
- Rapid Diagnostic Testing for HIV
- Impact of the New Guidelines for the Use of Antiretroviral Agents
- Community Based HIV Treatment Adherence Support
- Treatment of Tuberculosis in Patients Infected with HIV
- new topics frequently posted including AIDSLine CME

http://ccoe.umdnj.edu/online

AIDS Education and Training Centers (AETC) National Resource Center

www.aids-etc.org

HIV treatment guidelines and news, training materials and curricula, evaluation tools, and links to all AETCs.

Daily HIV/AIDS Treatment News [multi-source]:

http://www.aids-etc.org/aidsetc?page=et-14-00

Clinical Information Resources (new: PDA tools):

http://www.aids-etc.org/aidsetc?page=et-pda-00

NY/ NJ AETC

New York/ New Jersey regional training calendar, directory of HIV treatment and support resources; links and downloads for clinician support tools and treatment references including training slide sets and wall charts.

http://www.nynjaetc.org

STD/HIV Prevention Training Centers (PTC)

Part I [medical] CDC funded

http://www.nyc.gov/html/doh/html/std/ptc.shtml

Part II [Behavioral] CDC funded

www.urmc.rochester.edu/chbt

Addiction Technology Transfer Center (ATTC)

SAMHSA funded training, addiction treatment news

Northeast ATTC: http://www.neattc.org

Title X Family Planning Regional Training Center (RTC)

DHHS/OPA funded training: www.cicatelli.org/titlex/home.htm

HIV/AIDS Medical Update Series: Free On-site Training

Sponsors: Division of AIDS Education at UMDNJ-Center for Continuing and Outreach Education and the American Academy of CME, Inc., with funding from the NJ Department of Health & Senior Services, Division of HIV/AIDS Services.

Topics available:

- Diagnosis and Initial Management of HIV/AIDS: What the Primary Care Physician Should Know
- HIV/AIDS and Hepatitis C Co-Infection
- Immunizations for HIV Positive Adults
- Prevention and Prophylaxis for Occupational Exposure to HIV and Other Blood Borne Pathogens
- Prophylaxis and Treatment of Opportunistic Infections in Patients with HIV Disease
- HIV in Pregnancy - Preventing Perinatal Transmission
- Rapid Diagnostic HIV Testing

To schedule a free 1-hour HIV medical education program at your health care site on HIV/AIDS and Hepatitis C Co-Infection or any of the other topics in the HIV/AIDS Medical Update Series, contact Debra Bottinick at (609) 921-6622 or dbottinick@academycme.org.

2006 NIMH and IAPAC International Conference on HIV Treatment Adherence March 8-10, 2006

Jersey City, NJ: Hyatt Regency Hotel

Agenda, registration: www.hivadherenceconference.com

Sponsored by UMDNJ with the National Institute of Mental Health and the International Association of Physicians in AIDS Care

Late breaking abstracts accepted until January 17, 2006.

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